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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FLOOD, MICHELE C	
ART UNIT	**PAPER NUMBER**
1655	

DATE MAILED: 10/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/420,092	LUO ET AL.	
	Examiner	Art Unit	
	Michele Flood	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-17,20 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-17 and 20-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 28, 2005.

Acknowledgment is made of the receipt and entry of the declaration of Dr. Yasumichi Hitoshi filed under Rule 132.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 15-17 and 20-21 are under examination.

Response to Arguments

Claims 15-17 and 21 remain rejected under 35 U.S.C. § 101 because the claims are drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance.

Applicant's arguments and the declaration of Dr. Hitoshi filed under Rule 132 have been fully considered. However, the rejection stands for the reasons set forth in the previous Office action and for the reasons set forth below.

Applicant's main argument is directed to the idea that the present specification provides evidence that R0101 expression levels are upregulated in certain cancers when compared to non-cancerous tissues, and Applicant, as well as the declaration of Dr. Hitoshi, point to a post-filing reference to provide supporting evidence thereof. Applicant concludes that the application provides both an assertion of and evidence of utility of the claimed invention. However, Applicant's arguments are not persuasive. For instance, Applicant argues that the specification as filed, in combination with the post-filing reference (Yu et al., Oncology, 2001, 20: 484-489), demonstrates that overexpression of R0101 mRNA is associated with cancer, as well as the data shown in Figure 5 of the present application and the data shown in Figure 5 of Yu et al. are the same. However, the Office notes that Yu et al. merely suggest that $p15^{PAF}$ may be a new member of PCNA associated cell proliferation family of regulators which may possess prognostic significance in a broad array of human cancers. Furthermore, on page 485, under "*Discussion*", while Yu speculates that the overexpression of $p15^{PAF}$ in tumor tissues may advantageous for tumor cell proliferation, Yu also teaches that the full characterization of the biological function of $p15^{PAF}$ is still yet unknown and not wholly understood. For example, Yu teaches that the relative relationship between $p15^{PAF}$ and $p15^{21}$ is unknown. Furthermore, Yu asserts, "An *in vitro* DNA synthesis assay may be need to reveal the detailed mechanism of $p15^{PAF}$ function."

Next, Applicant argues that there is no predetermined amount of evidence that must be provided to support utility. Again, Applicant points to the teachings of Yu et al. to demonstrate that one of skill would consider the asserted utility to be more likely than not true. Full consideration was given to the teachings of Yu' reference. However, Applicant is reminded that a post-filing reference cannot be relied upon to provide evidential support of utility for a claimed invention. Nonetheless, even in view of the Yu' reference, the Office notes that while Yu teaches a significant increase in expression of $p15^{PAF}$ in several types of tumor tissues, the Office also notes that Yu merely suggests that $p15^{PAF}$ may possess a prognostic parameter for certain types of cancers. Even Yu clearly points out that the biological function of $p15^{PAF}$ is unknown, on page 486, Column 2, lines 2-4. Thus, while Applicant argues that "all that is required is a reasonable correlation between the asserted use and biological activity", the Office maintains that it is clear from the post-filing reference of Yu and from the present specification that the protein described therein is what is termed an "orphan protein" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed

the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", " [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", " [i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a protein of as yet undetermined function or biological significance. The claims are drawn to an isolated alleged cell cycle protein R0101 encoding Seq. ID No.: 2. The instant specification discloses that the claimed amino acid sequence can be employed to screen bioactive agents, when the cell cycle protein R0101 is combined with a bioactive agent by determining the binding capacity of the bioactive agent to the said alleged cell cycle protein R0101 (Seq. ID No.: 2). The specification discloses that such a screening assay can be employed to identify compounds, which act as modulators of cell cycle activity. The instant application discloses that there is a plurality of different modulators that promote, enhance or deter inhibitors of cell proliferation and that the identification of such cell cycle components and modulators is highly desirable for the therapeutic use thereof. The instant specification further discloses that there is a plurality of different mammalian proteins,

which are known to function as alleged cell cycle proteins. However, neither the instant specification nor the art of record identifies even a single disease or disorder that has been shown to be associated with alleged cell cycle protein R0101, the claimed amino acid and the protein encoded thereby can not be employed in either a screening or diagnostic capacity. For instance, Applicant asserts that the instant R0101 (Seq. ID No.: 2) as an alleged cell cycle protein without providing any evidence or examples to support such a conclusion. Thus, Applicant's assertion appears to be purely speculative and wholly unsupported by any evidence of record. Since the prior art indicates a mere 14% amino acid sequence identity to a protein without an established function of the instantly claimed alleged cell cycle protein R0101 encoding Seq. ID No.: 2, one of ordinary skill in the art would not reasonably extrapolate or conclude a common function between structurally dissimilar proteins, much less one having 95% amino acid sequence identity to the amino acid sequence set forth in Seq. ID No.: 2 as instantly claimed by Applicant. Neither the instant specification nor the art of record clearly identifies a single disease or disorder that has been shown to be associated with alleged cell cycle protein R0101 of the instant invention. Since the alleged cell cycle protein R0101 of the instant invention has not been shown to be associated with a particular physiological process that an artisan would wish to manipulate for assaying bioactive agents for the identification of compounds which bind thereto, the claimed alleged cell cycle protein R0101 can not be used to identify compounds which would have the clinical effect of modulating processes of the cell cycle or which would be ultimately employed in a diagnostic capacity and therapeutic use thereof. Until some actual and specific significance can be attributed to the protein identified in the

specification as alleged cell cycle protein R0101 (Seq. ID No.: 2), or the gene encoding it, the instant invention is incomplete. The protein encoded by a DNA of the instant invention is a compound known to be structurally analogous to proteins which are known in the art as alleged cell cycle proteins. In the absence of a knowledge of the natural ligands or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of bioactive agents capable of binding to the said alleged cell cycle protein R0101 is clearly to use it as the object of further research which has been determined by the courts to be a utility which, alone, does not support patentability.

While Applicant continues to argue that the specification shows to one of ordinary skill in the art that R0101 is associated with certain cancers as set forth in Figure 5, the Office notes that there is nothing in the rendering of Figure 5 or the description of Figure 5 on page 4 of the specification, line 6, that would indicate the nexus between the overexpression of R010 alleged cell cycle protein in cancerous cell types and the use of R010 protein as a target to identify agents that bind thereto for either diagnostic or prognostic screening assays for cancer. For instance, it is unclear from any of the illustrated figures whether Applicant shows protein binding, nucleic acid or mRNA binding to any of the cell types. Moreover, it is unclear as to whether the overexpression of R010 in certain cancerous disease conditions is a protein marker indicative of cancer or whether the associated overexpression of the R010 protein is merely a result of an increase in metabolic protein activity. Although Applicant continues to argue that the claimed screening method has utility for the routine identification of bioactive agents that bind to R010 protein, *i.e.*, for the diagnosis of, or

prognostic evaluation of cancer, the Office maintains that since the instant specification does not disclose a credible "real world" use for alleged cell cycle protein R0101 then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Hence, Claims 15-17 and 20-21 as amended remain rejected under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. § 101.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-17 and 20-21 as amended remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's arguments and the declaration of Dr. Hitoshi filed under Rule 132 have been fully considered. However, the rejection stands for the reasons set forth in the previous Office action and for the reasons set forth below.

Applicant argues that there is no requirement in U.S. Code, case law, or regulations that a claimed protein must correspond to a previously known protein with known activity in order to meet the enablement requirement. Applicant further argues

that the specification provides the protein sequence of R0101, the activity of R0101, and correlates R0101 overexpression with the disease cancer. Thus, Applicant concludes that the specification fulfills the "how to use" portion of the enablement requirement. Moreover, Applicant argues that the specification discloses binding assays that would enable one of skill in the art to practice the instantly claimed invention without undue experimentation; and, thus Applicant points to Figures 2, 5, 8 and 9 to provide support for Applicant's assertion. However, as set forth above, Applicant's assertion is not enabled because there is no way of determining whether the protein corresponding to (Seq. ID No.: 2) corresponds to any known protein with known activity, but for which the sequence is unknown. Therefore, the broad concept of using a alleged cell cycle protein with (Seq. ID No.: 2) in a screening assay for determining the binding of candidate bioactive agents to the alleged cell cycle protein R0101 is clearly beyond the skill of one of ordinary skill in the art, requiring enormous burden and experimentation without a reasonable expectation of success. The Office maintains that overexpression of the mRNA protein could mean that it is a metabolically active protein, instead of being associated with a protein which is associated with or disease causing; and, thus it would be expected that the mRNA expression would be elevated. Again, the Office notes that neither Applicant nor the post-filing reference of Yu teaches a clear biological function of $p15^{PAF}$.

Because Applicant has not established a substantial and credible nexus between the overexpression of alleged cell cycle protein R0101 and the occurrence of cancerous cell types, it is unclear as how one would be able to determine the meaning for the

binding of alleged cell cycle protein R0101 to any candidate bioactive agent. Speculation does not constitute enablement.

Claims 15-17 and 20-21 as amended remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's arguments and the declaration of Dr. Hitoshi filed under Rule 132 have been fully considered. However, the rejection stands for the reasons set forth in the previous Office action and for the reasons set forth below.

With respect to the rejection made in the previous Office action under written description, Applicant argues that the declaration of Dr. Hitoshi provides support that the specification as written is sufficient for those of skill to practice the claimed invention. Applicant further argues that the specification provides description of binding assays and description of hybrid assays and argues that the specification does provide the required description of the claimed assays for screening for a bioactive agent that binds to R0101. However, Applicant's arguments are not persuasive because a mere listing of binding assays to describe a method for screening for a bioactive agent capable of binding to a alleged cell cycle protein comprising combining the alleged cell cycle protein and a candidate bioactive agent generally known to exist, in the absence of knowledge as how to determine whether binding has occurred between the alleged cell cycle protein and the bioactive agent is not a description of the material or the method

of use thereof. The Office maintains that the mere disclosure that those skilled in the art would know how to perform the instantly claimed invention for the determination of binding of ingredients, the modulation of cell cycle activity, and detection of cell cycle regulation is not an adequate description of the claimed invention. For instance, nowhere in the present specification does Applicant disclose a description for the experimentation of combining the disclosed R0101 alleged cell cycle protein with a candidate bioactive agent, and determining whether binding between the two ingredients has occurred. Nowhere in the present specification does Applicant provide a teaching as to how one of either ordinary skill in the art or those skilled artisan would determine whether binding has occurred, since Applicant has not adequately defined or given an example of a binding event. While Applicant argues that the specification discloses that Applicants have isolated a nucleic acid that encodes R0101 protein (*i.e.,* SEQ ID NO:1) and provide both the nucleic acid and the encoded amino acid (*i.e.,* SEQ ID NO:2), it is unclear as how one would properly interpret the subject matter Applicant intends to direct the invention since Applicant provides no explanation of the experiments that have been performed or the significance of the binding activity disclosed in the present specification. Thus, it is uncertain as to what a method for screening for a bioactive agent that binds a cell cycle protein, wherein the protein comprises an amino acid sequence having at least about 95% identity to SEQ ID NO:2, comprising binding a candidate bioactive agent that binds to proliferating PCNA and determining the binding of the candidate bioactive agent to cell cycle protein R010

would show, given that no biological function has been assigned to the instantly claimed cell cycle protein.

Thus, Claims 15-17 and 20-21 as amended remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The broad generic claim lacks sufficient description to inform a skilled artisan that Applicant was in possession of the claimed invention at the time of filing since the specification lacks a sufficient number of species which have been described by complete structure or identifying characteristics, thus the description requirement has not been satisfied, see Eli Lilly, 119 F. 3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1977).

No claims are allowed.

Conclusion

This is a Request for Continued Examination of applicant's earlier Application No. 09/420,092. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele Flood whose telephone number is 571-272-0964. The examiner can normally be reached on 7:00 am - 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michele C. Flood

MICHELE FLOOD
PRIMARY EXAMINER

Michele Flood
Primary Examiner
Art Unit 1655

MCF
October 14, 2005